Remarks

The present invention is directed to methods of delaying or reducing the progression of Alzheimer's disease. Claims 1-18 have been cancelled. Claims 19-27 are currently pending. Claims 21 and 22 are withdrawn from consideration. Claim 19 has been amended. Claims 28-30 have been newly added. Support for this amendment and new claims is found in the specification for example at page 6, lines 31-33; page 5, line 14; and page 23, lines 19-21.

Rejections under 35 U.S.C. 112 first paragraph (enablement)

Claims 19, 20 and 23-27 are rejected under 35 U.S.C. 112, first paragraph, because the Examiner asserts that the specification does not reasonably provide enablement for methods of treating Alzheimer's disease. The Examiner indicated in the Office Action at page 3 that the application is enabling for methods of enhancing antigenicity by administering the supramolecular antigenic construct described in the specification.

Claim 19 has been amended to now recite a method for "….*enhancing antigenicity in a patient suffering from Alzheimer's disease comprising administering to a patient in need thereof a supramolecular antigenic construct reconstituted in a liposome.*"
Support for this amendment can be found, for example, on page 6, lines 31-33 in combination with page 5, line 14 of the application as filed.

Applicants have described such methods in the specification and have provided working examples demonstrating the immunogenicity of the supramolecular constructs described in the specification. Applicants assert that the specification provides sufficient guidance to enable one of ordinary skill in the art to use the claimed methods of administering the disclosed

supramolecular constructs in manner correlated with the scope of the claims. Therefore Applicants respectfully request withdrawal of this rejection.

The Examiner has also rejected claim 27 for lacking enablement for treating Alzheimer's disease, multidrug resistance in cancer cells or prion diseases. Claim 27 has been cancelled thereby rendering this rejection moot.

Rejections under 35 U.S.C. 112 first paragraph (written description)

Claims 19, 20 and 23-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner has indicated that the claims allegedly read on any antigenic polypeptide from any amyloid protein. Furthermore, the Examiner has stated that, contrary to the Applicants assertion and due to the use in the claim of the open phrase "*..having*", the claimed peptide is not limited to β-amyloid or fragments thereof but includes any antigenic polypeptide that encompasses the fragment of β-amyloid and other unspecified amino acid sequences in addition to the β-amyloid sequence.

Claim 19 has been amended to replace the objected phrase "having" with "consisting of". Reconsideration and withdrawal of the Examiner's rejection is respectfully requested in view of the above amendment.

Rejections under 35 U.S.C. 102(b)

Claims 19, 20 and 23-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Nicolau et al., PNAS, 2002 vol. 99, no. 4, p. 2332-2337 ("Nicolau"). Applicants respectfully traverse the rejection as it applies to the amended claims.

Nicolau teaches the administration of a palmitoylated β-amyloid peptide to reduce the

presence of β-amyloid plaques in the pancreas of transgenic NORBA mice. Nicolau fails to teach an increase in levels of memory restoration and curiosity awakening as compared to levels prior to administration as recited in the amended claims. Therefore, Nicolau et al. fails to anticipate the claimed methods.

The Examiner has disregarded Applicants' argument that Nicolau et al. express serious doubt to the relevance of the NORBA mouse model for the treatment of Alzheimer's diseases because the NORBA model does not provide a blood-brain barrier to cross for the antibodies to reach the pancreatic plaques and further that Nicolau et al. fails to provide any evidence that the compound would be able to act on plaque deposition in the brain or reduce symptoms of AD.

The Examiner has stated that Nicolau et al. suggest different mechanisms of destruction of plaques including opsonization of the plaques and the subsequent destruction by microglia macrophages, alteration of the transport and equilibrium of β-amyloid between brain and plasma and direct interaction of β-amyloid antibodies with the plaque.

Contrary to the Examiner's above assertion, Nicolau et al does not provide any evidence that the antigenic construct disclosed in this paper uses any of these alternatives for clearing plaques from the brain, except the last one which is based on the direct interaction of β-amyloid antibodies with the plaque. In particular, Nicolau et al state in the first full paragraph on page 2337, right column, that "*…our own in vitro data (Fig. 4A) suggest that direct interaction of anti-Aβ antibodies with Aβ aggregates induces extensive solubilization of the latter.*" *and further that "On the basis of available data, it is difficult to select which is the principal mechanism, but all three mechanisms may be involved.*"

From the above statement it is evident that the data provided by Nicolau et al only support the 3rd alternative of making use of the direct interaction of β-amyloid antibodies with

the plaque. However, for this to happen the antibodies must cross the blood brain barrier in order to be able to get into contact with the plaque deposits in the brain of Alzheimer patients. Clearly, just clearing plaques from the pancreas as shown by Nicolau et al would not result in increased levels of memory restoration and curiosity awakening as now recited in the claims.

Applicants assert that for the above reasons and in view of the amendments to the claims, Nicolau et al neither anticipates nor renders obvious the claimed method of enhancing antigenicity in a patient suffering from Alzheimer's disease comprising administering to a patient in need thereof a supramolecular antigenic construct of the invention, which enhanced antigenicity leads to increased levels of memory restoration and curiosity awakening in the treated patients.

The Examiner has also asserted that the composition referenced in Nicolau et al inherently delays or reverses the progression of Alzheimer's diseases by enhancing antigenicity. In particular, the Examiner asserts, that even "…. *if the claimed method does not recite a particular patient population, the patient population having Aβ plaques cannot be excluded from the study because having Aβ plaques is considered as indication of Alzheimer's disease (p. 2332).*"

It is unclear which passage the Examiner is actually referring to on page 2332. It appears that the Examiner is suggesting that a patient having Aβ plaques necessarily suffers from Alzheimer's Disease irrespective of where these plaques are located. However, Applicants submit that there is no evidence in Nicolau et al or in any other document on record that would support the Examiner's allegation. To the contrary, Nicolau et al explicitly state on page 2332 (left column, 1st full paragraph after the Abstract) that "*One of the major pathological features of AD is the abundant presence of amyloid plaques* ***in the brain*** *of affected individuals.*" [emphasis

added] and further that "*The frequency and distribution of the neurofibrillary tangles and of the neurite plaques appear to correlate well with the extent of cognitive impairment and other characteristic symptoms.*"

The above statement does not leave much room for the Examiner's interpretation alleging that the mere presence of plaques irrespective of where they occur would be an indication of Alzheimer's Disease. Furthermore, Applicants also note that if the Examiner's inherency argument is a valid argument to make, this position would prevent patenting of any second medical use indication for a known medicament.

In view of the amendments that have been effected in the claims and the remarks provided above, reconsideration and withdrawal of the Examiner's §102 rejection is respectfully requested.

Conclusions

Applicants submit that the response herein provides a complete response to the Office Action dated March 24, 2009.

If the Examiner believes there are other issues that may be resolved by telephone interview, or that there are any informalities remaining in the application that may be corrected by Examiner's Amendment, a telephone call to the undersigned is respectfully solicited.

No additional fees are believed due, however the Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment of fees to Deposit Account number 50-5193.

Respectfully submitted,

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